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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/394,020	09/10/1999	CARMEN V. PEPICELLI	HUIP-P01-032	3626

28120 7590 11/23/2001

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EXAMINER

ANDRES, JANET L

ART UNIT PAPER NUMBER

1646

DATE MAILED: 11/23/2001

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Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/394,020

Applicant(s)

PEPICELLI ET AL.

Examiner

Janet L Andres

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 10 September 2001.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-32 is/are pending in the application.
- 4a) Of the above claim(s) 18-21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-17, 22-32 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

### **RESPONSE TO AMENDMENT**

1. Applicant's amendment and declaration under 35 U.S.C. 1.132, filed 10 September 2001, are acknowledged. Claims 1-32 are pending in this application. Claims 18-21 are withdrawn from consideration as being drawn to a non-elected invention. The claims are examined in light of Applicant's election of hedgehog therapeutics in paper no. 23.

2. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

#### ***Claim Rejections/Objections Withdrawn***

3. The rejection of claim 1 under 35 U.S.C. 112, second paragraph, as indefinite in the recitation of "ectopically contacting" is withdrawn in response to Applicant's amendment.

The rejection of claim 15 under 35 U.S.C. 112, second paragraph, as indefinite in the recitation of "encodable" and of hybridization conditions is withdrawn in response to Applicant's argument.

The rejection of claims 1-17 under 35 U.S.C. 112, second paragraph, as indefinite in the recitation of "growth state" and "therapeutic" is withdrawn in response to Applicant's amendment.

The rejection of claims 6-17 under 35 U.S.C. 112, second paragraph, as indefinite in the recitation of "bioactive" is withdrawn in response to Applicant's amendment.

#### ***Claim Rejections Maintained/New Grounds of Rejection***

4. The rejection of claims 1-17 under 35 U.S.C. 112, first paragraph, is maintained and applied to new claims 22-32.

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4a. Applicant argues that the role of hedgehog signalling has been extensively studied in numerous developmental contexts. Applicant further argues that the specification provides extensive support for a role for hedgehog signalling in lung development.

Applicant's arguments have been fully considered but have not been found to be persuasive. As stated in the previous office action, there is no nexus provided between the role of the protein in differentiation and its use as a therapeutic agent. Development is a complex process involving the interactions of many factors and cell types as well as both temporal and spatial concerns; the function of any particular agent in any condition in developed animal is not readily predictable from its roles in development.

4b. Applicant argues that the specification provides guidance for the use of ptc, hedgehog, or FGF-10 therapeutics for the treatment of lung cancer. Applicant cites additionally the work of Fujita et al. as indicating that Shh is expressed in lung squamous carcinoma cell lines and in some adenocarcinoma lines. Applicant cites MPEP as stating that an example may be working or prophetic.

Applicant's arguments have been fully considered but have not been found to be persuasive. The claims as written encompass not only cancer but also any form of modulation of proliferation, differentiation, or survival of lung tissue, as well as inducing the formation of, maintenance of and functional performance of lung tissue. Thus the possibility that hedgehog inhibition might be useful in the treatment of lung cancer is not sufficient guidance to enable the invention as broadly claimed. The claims encompass forms of modulation very different than inhibition of growth. Furthermore, the teachings of Fujita et al. indicate that Shh is not expressed in all lung cancers. Thus one of skill would not predictably be able to use hedgehog

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inhibitors, or any other of the claimed agents, even to inhibit lung cancers. While working examples are not required, what is required is sufficient guidance to allow the predictable use of the invention as claimed. Here, one of skill in the art would not be able, based on the guidance provided, to predictably use hedgehog antagonists to modulate proliferation, differentiation, and function of lung tissue as broadly claimed. Since Applicant elected hedgehog therapeutics in paper no. 23, ptc and FGF-10 effectors are not under consideration in this application..

4c. Applicant's declaration indicates that inhibition of hedgehog signalling promotes surfactant production. Applicant suggests that inhibition of hedgehog signalling might therefore be a therapeutic agent for neonatal respiratory distress syndrome. However, as stated above, the claims encompass any and all forms of modulation of lung tissue. The induction of surfactant production is further not an indicator of cell differentiation; markers may be expressed without actual differentiation. In addition, surfactant production does not indicate to one of skill that the inhibitor could successfully be used to treat even RDS, since RDS could be caused by deficiency in the ability to produce surfactant, which would not be affected by Applicant's invention. Finally, surfactant production and treatment of RDS are not addressed in the original specification. While post-filing date evidence may be used to establish enablement, Applicant's subsequent data encompass a disease and function different from that contemplated in the specification, and thus do not indicate that the invention was enabled at the time of filing.

5. Claims 16 and 17 are newly rejected under 35 U.S.C. 112, second paragraph. These claims depend from claim 6, which is drawn to methods using antagonists, but require the use of molecules which appear from the specification to be agonists.

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NO CLAIM IS ALLOWED.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet Andres, Ph.D., whose telephone number is (703) 305-0557. The examiner can normally be reached on Monday through Friday from 8:00 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, Ph.D., can be reached at (703) 308-6564. The fax phone number for this group is (703) 305-3014 or (703) 308-4242.

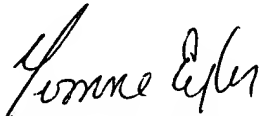
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Communications via internet mail regarding this application, other than those under U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [yvonne.eyler@uspto.gov].

All Internet email communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark Office on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Janet Andres, Ph.D.  
November 19, 2001

  
YVONNE EYLER, PH.D  
SUPERVISORY PATENT EXAMINER  
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